Amendments to the Claims

Please amend Claims 11, 12, 35-37 and 39-43. Please add Claim 44. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

Claim 1 (original): A method of stimulating bone growth at a site in a subject in need of osteoinduction, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor.

Claim 2 (original): The method of Claim 1 wherein the site is in need of a bone graft.

Claim 3 (original): The method of Claim 1 wherein the site is a segmental gap in a bone, a bone void or at a non-union fracture.

Claim 4 (previously presented): The method of Claim 1 wherein the agonist is a thrombin peptide derivative, or a physiologically functional equivalent thereof, comprising a polypeptide represented by the following structural formula:

Asp-Ala-R;

wherein R is a serine esterase conserved sequence.

Claim 5 (previously presented): The method of Claim 4 wherein the agonist consists of between about 12 and about 23 amino acids.

Claim 6 (withdrawn): The method of Claim 5 wherein the serine esterase conserved sequence consists of the amino acid sequence of SEQ ID: NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a C-terminal truncated fragment thereof consisting of at least six amino acids, provided that zero, one, two or three

amino acids in the serine esterase conserved sequence differ from the corresponding position of SEQ ID: NO. 1.

Claim 7 (withdrawn): The method of Claim 5 wherein the serine esterase conserved sequence consists of the amino acid sequence of SEQ ID: NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a C-terminal truncated fragment thereof consisting of at least nine amino acids, provided that zero, one or two of the amino acids in the serine esterase conserved region are conservative substitutions of the corresponding amino acid in SEQ ID: NO. 1.

Claim 8 (withdrawn): The method of Claim 5 wherein the serine esterase conserved sequence consists of the amino acid sequence of SEQ ID: NO. 2 (Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val, wherein X1 is Glu or Gln and X2 is Phe, Met, Leu, His or Val), or a C-terminus truncated fragment of SEQ ID: NO. 2, said fragment consisting of at least six amino acids.

Claim 9 (withdrawn): The method of Claim 8 wherein the agonist comprises the amino acid sequence Arg-Gly-Asp-Ala (SEQ ID: NO. 3).

Claim 10 (withdrawn): The method of Claim 9 wherein the agonist comprises the amino acid sequence Arg-Gly-Asp-Ala-Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val (SEQ ID: NO. 4), wherein X1 is Glu or Gln and X2 is Phe, Met, Leu, His or Val.

Claim 11 (currently amended): The method of Claim 4 ~~Claim 10~~ wherein the agonist consists of the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- ~~(SEQ ID: NO. 5)~~ (SEQ ID NO.:5), or an N-terminal truncated fragment thereof, provided that zero, one, two or three amino acids at positions 1-9 in the agonist differ from the amino acid at the corresponding position of ~~SEQ ID: NO. 5~~ SEQ ID NO.: 5.

Claim 12 (currently amended): The method of Claim 4 ~~Claim 10~~ wherein the agonist consists of the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- ~~(SEQ ID. NO. 5)~~ (SEQ ID NO.: 5), or an N-terminal truncated fragment thereof, provided that zero, one or two amino acids at positions 1-9 in the agonist are conservative substitutions of the amino acid at the corresponding position of ~~SEQ ID. NO. 5~~ SEQ ID NO.: 5.

Claim 13 (previously presented): The method of Claim 11 wherein the agonist is administered in a pharmaceutical composition additionally comprising an implantable, biocompatible carrier.

Claim 14 (original): The method of Claim 13 wherein the implantable, biocompatible carrier is an osteoconductive matrix.

Claim 15 (original): The method of Claim 11 wherein the carrier comprises a polylactic acid/polyglycolic acid homopolymer or copolymer.

Claim 16 (original): The method of Claim 1 wherein the subject is a farm animal, a companion animal or a laboratory animal.

Claim 17 (withdrawn): A pharmaceutical composition comprising an implantable, biocompatible carrier and an agonist of the non-proteolytically activated thrombin receptor.

Claim 18 (withdrawn): The pharmaceutical composition of Claim 17 wherein the carrier is osteoconductive.

Claim 19 (withdrawn): The pharmaceutical composition of Claim 18, wherein the thrombin receptor agonist is a thrombin peptide derivative, or a physiologically functional

equivalent thereof, comprising a polypeptide represented by the following structural formula:

Asp-Ala-R;

wherein R is a serine esterase conserved sequence.

Claim 20 (withdrawn): The pharmaceutical composition of Claim 19 wherein the carrier is a biodegradable synthetic polymer.

Claim 21 (withdrawn): The pharmaceutical composition of Claim 20 wherein the biodegradable synthetic polymer is a polylactic acid/polyglycolic acid homopolymer or copolymer.

Claim 22 (withdrawn): The pharmaceutical composition of Claim19 wherein the carrier comprises collagen, fibrin, calcium phosphate salts, calcium sulfate, guanidine-extracted allogenic bone or a combination thereof.

Claim 23 (withdrawn): The pharmaceutical composition of Claim19 wherein the carrier is injectable.

Claim 24 (withdrawn): The pharmaceutical composition of Claim 23 wherein the carrier is a poly(propylene fumarate) solution or a calcium phosphate ceramic paste.

Claim 25 (withdrawn): The pharmaceutical composition of Claim19 wherein the pharmaceutical composition is administered as microparticles.

Claim 26 (withdrawn): The pharmaceutical composition of Claim19 wherein the pharmaceutical composition is pre-shaped before applying to the site in need of osteoinduction.

Claim 27 (withdrawn): The pharmaceutical composition of Claim19 wherein the agonist consists of between about 12 and about 23 amino acids.

Claim 28 (withdrawn): The pharmaceutical composition of Claim 27 wherein the serine esterase conserved sequence consists of the amino acid sequence of SEQ ID: NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a C-terminal truncated fragment thereof consisting of at least six amino acids, provided that zero, one, two or three amino acids in the serine esterase conserved sequence differ from the corresponding position of SEQ ID: NO. 1.

Claim 29 (withdrawn): The pharmaceutical composition of Claim 27 wherein the serine esterase conserved sequence consists of the amino acid sequence of SEQ ID: NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a C-terminal truncated fragment thereof consisting of at least nine amino acids, provided that zero, one or two of the amino acids in the serine esterase conserved sequence are conservative substitutions of the corresponding amino acid in SEQ ID: NO. 1.

Claim 30 (withdrawn): The pharmaceutical composition of Claim 27 wherein the serine esterase conserved sequence consists of the amino acid sequence of SEQ ID: NO. 2 (Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val) , wherein X1 is Glu or Gln and X2 is Phe, Met, Leu, His or Val), or a C-terminus truncated fragment of SEQ ID: NO. 2, said fragment consisting of at least six amino acids.

Claim 31 (withdrawn): The pharmaceutical composition of Claim 30 wherein the agonist comprises the amino acid sequence Arg-Gly-Asp-Ala (SEQ ID: NO. 3).

Claim 32 (withdrawn): The pharmaceutical composition of Claim 31 wherein the agonist comprises the amino acid sequence Arg-Gly-Asp-Ala-Cys-X_1-Gly-Asp-Ser-Gly-Gly-Pro-X_2-Val (SEQ ID: NO. 4), wherein X_1 is Glu or Gln and X_2 is Phe, Met, Leu, His or Val.

Claim 33 (withdrawn): The pharmaceutical composition of Claim 32 wherein the agonist consists of the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID: NO. 5), or an N-terminal truncated fragment thereof, provided that zero, one, two or three amino acids at positions 1-9 in the agonist differ from the amino acid at the corresponding position of SEQ ID: NO. 5.

Claim 34 (withdrawn): The pharmaceutical composition of Claim 32 wherein the agonist consists of the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID: NO. 5), or an N-terminal truncated fragment thereof, provided that zero, one or two amino acids at positions 1-9 in the agonist are conservative substitutions of the amino acid at the corresponding position of SEQ ID: NO. 5.

Claim 35 (currently amended): A method of stimulating bone growth at a site in a subject in need of osteoinduction, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, said agonist ~~a peptide~~ consisting of the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val ~~(SEQ ID: NO. 5)~~ (SEQ ID NO.: 5).

Claim 36 (currently amended): A method of stimulating bone growth at a site in need of a bone graft in a subject, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, said agonist ~~a peptide~~ consisting of the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val ~~(SEQ ID: NO. 5)~~ (SEQ ID NO.: 5).

Claim 37 (currently amended): A method of stimulating bone growth in a subject at a segmental bone gap, a bone void or a non-union fracture, said method comprising

the step of administering to the bone gap, bone void or nonunion fracture a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, said agonist ~~a peptide~~ consisting of the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val ~~(SEQ ID: NO. 5)~~ (SEQ ID NO: 5).

Claim 38 (previously presented): The method of Claim 5, wherein the agonist comprises a C-terminal amide.

Claim 39 (currently amended): The method of Claim 5, wherein the agonist comprises Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH_2 ~~(SEQ ID: NO. 6)~~ (SEQ ID NO.: 6).

Claim 40 (currently amended): The method of Claim 5, wherein the agonist consists of Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH_2 ~~(SEQ ID: NO. 6)~~ (SEQ ID NO.: 6).

Claim 41 (currently amended): A method of stimulating bone growth at a site in a subject in need of osteoinduction, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, said agonist consisting of the sequence of Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH_2 ~~(SEQ ID: NO. 6)~~ (SEQ ID NO.: 6).

Claim 42 (currently amended): A method of stimulating bone growth at a site in need of a bone graft in a subject, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, said agonist consisting of the sequence of Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-

Pro-Phe-Val-NH_2 ~~(SEQ ID. NO. 6)~~ (SEQ ID NO.: 6), or an N-terminal truncated fragment thereof.

Claim 43 (currently amended): A method of stimulating bone growth at a segmental bone gap, a bone void or a non-union fracture, said method comprising the step of administering to the bone gap, bone void or non-union fracture a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, said agonist consisting of the sequence of Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH_2 ~~(SEQ ID. NO. 6)~~ (SEQ ID NO.: 6).

Claim 44 (new): The method of Claim 5, wherein the agonist comprises Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH_2 (SEQ ID NO.: 6).